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Ethyl 5-methyl-7-phenyl-1,2,4-triazolo-[4,3-*a*]pyrimidine-6-carboxylate

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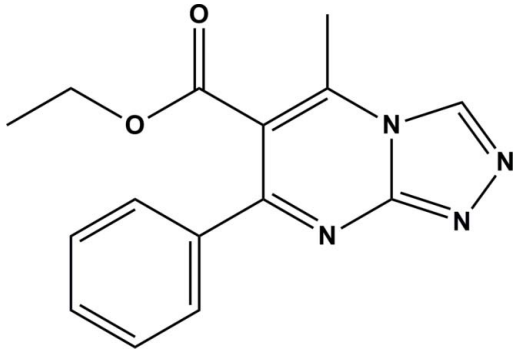
Key indicators: single-crystal X-ray study; T = 293 K; mean σ(C–C) = 0.004 Å; R factor = 0.076; wR factor = 0.182; data-to-parameter ratio = 13.2.

In the title compound, $C_{15}H_{14}N_4O_2$, the triazolopyrimidine ring system is almost planar (r.m.s. deviation = 0.02 Å) and the phenyl ring is inclined to its mean plane by 42.45 (9)°. The carboxyl group is inclined to the triazolopyrimidine ring mean plane by 57.8 (3)°. In the molecule, there is a short C—H···O contact involving the carbonyl O atom and an H atom of the adjacent methyl substituent. In the crystal, neighbouring molecules are linked by C—H···O hydrogen bonds, forming chains propagating along [010]. There are also weak π–π interactions present involving the pyridine and phenyl rings of neighbouring chains [intercentroid distance = 3.8580 (16) Å].

Related literature

For information on annelated pyrimidine derivatives as promising vasodilating agents, see: Jeanneau-Nicolle *et al.* (1992); Ali *et al.* (2011). For details concerning triazolopyrimidines having antihypertensive and diuretic activity, see: Ali *et al.* (2011). For details of Biginelli dihydropyrimidine calcium channel blockers, see: Rovnyak *et al.* (1995); Triggle & Padmanabhan (1995); Ohno *et al.* (2002). For potential *ex vivo* calcium-channel-blocking activity, see: Farghaly *et al.* (2013).



Experimental

Crystal data

$C_{15}H_{14}N_4O_2$
M_r = 282.30
Monoclinic, $P2_1/n$
a = 10.322 (2) Å
b = 8.1678 (19) Å
c = 16.798 (4) Å
β = 92.111 (4)°
V = 1415.2 (5) Å^3
Z = 4
Mo $K\alpha$ radiation
μ = 0.09 mm^{-1}
T = 293 K
0.30 × 0.10 × 0.10 mm

Data collection

Rigaku SCXmini diffractometer
Absorption correction: multi-scan (*REQAB*; Jacobson, 1998)
T_{min} = 0.610, T_{max} = 0.991
12066 measured reflections
2550 independent reflections
1742 reflections with $I > 2\sigma(I)$
R_{int} = 0.092

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.076
$wR(F^2)$ = 0.182
S = 1.07
2550 reflections
193 parameters
H-atom parameters constrained
$\Delta\rho_{max}$ = 0.46 e Å^{-3}
$\Delta\rho_{min}$ = −0.51 e Å^{-3}

Table 1
Hydrogen-bond geometry (Å, °).

D—H···A	D—H	H···A	D···A	D—H···A
C9—H9B···O2	0.96	2.58	3.127 (4)	116
C15—H15···O2^{i}	0.93	2.57	3.246 (3)	129

Symmetry code: (i) $x, y-1, z$.

Data collection: *PROCESS-AUTO* (Rigaku, 1998); cell refinement: *PROCESS-AUTO*; data reduction: *CrystalStructure* (Rigaku Americas and Rigaku, 2007); program(s) used to solve structure: *SIR88* (Burla *et al.*, 1989); program(s) used to refine structure: *SHELXL2013* (Sheldrick, 2008); molecular graphics: *PLATON* (Spek, 2009) and *CrystalStructure* (Rigaku Americas and Rigaku, 2007); software used to prepare material for publication: *SHELXL2013* and *CrystalStructure*.

Supporting information for this paper is available from the IUCr electronic archives (Reference: SU2724).

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supporting information

Acta Cryst. (2014). E**70**, o672–o673 [doi:10.1107/S1600536814010113]

Ethyl 5-methyl-7-phenyl-1,2,4-triazolo[4,3-*a*]pyrimidine-6-carboxylate

Omaima M. AboulWafa, Ahmed M. Farghaly, Mohamed Teleb and Khaled S. Sinoussy

S1. Introduction

Annelated pyrimidine derivatives have gained considerable interest as promising vasodilating agents (Jeanneau-Nicolle *et al.*, 1992; Ali *et al.*, 2011). Triazolopyrimidines in particular have shown antihypertensive as well as diuretic activities (Ali *et al.*, 2011). The title compound has a triazolopyrimidine nucleus and was derivatized from the well known Biginelli dihydropyrimidine calcium channel blockers (Rovnyak *et al.*, 1995; Triggle & Padmanabhan, 1995; Ohno *et al.*, 2002). It has been shown to possess potential ex vivo calcium channel blocking activity (Farghaly *et al.*, 2013). In the present investigation, the crystal structure of the title compound was obtained in an effort to gain information pertaining to the role of regiocontrol in the cyclization step as well as electronic induction in the conformation of such a molecule.

S2. Discussion

The stereochemistry of the title compound, Fig. 1, revealed that the product has retained its original stereochemistry, and that cyclization has occurred on N^1 as predicted from HMBC (Heteronuclear Multiple Bond Correlation experiment). A close contact between the ester moiety and the phenyl group is also evident.

In the title compound, the triazolopyrimidine ring system is planar [r.m.s. deviation 0.02 Å] and its mean plane is inclined to the phenyl ring (C10—C15) by 42.45 (9) °. The carboxyl group (COO) is inclined to the triazolopyrimidine ring mean plane by 57.8 (3) °. It occupies a *cis* position relative to C5═C6 double bond of the triazolopyrimidine ring system thus allowing potential stabilization of such a conformation. There is a short C—H···O contact involving atom O2 and an H atom of the adjacent methyl substituent (C9), see Table 1. The ester group is again oriented away from the phenyl ring substituent for steric considerations with a torsional angle C4—C5—C6—O1 = -56.1 (3)°.

In the crystal, neighbouring molecules are linked by C—H···O hydrogen bonds forming chains propagating along [010]; Table 1 and Fig. 2. There are also weak π-π interactions present involving the pyridine and phenyl rings of neighbouring chains [Cg2—$Cg3^{i}$ = 3.8580 (16) Å; Cg2 and Cg3 are the centroids of rings N1/N2/C2—C5 and C10—C15, respectively; symmetry code: (i) -x+3/2, y+1/2, -z+1/2].

S3. Experimental

S3.1. Synthesis and crystallization

A solution of ethyl 2-hydrazino-6-methyl-4-phenylpyrimidine-5-carboxylate (0.27 g, 1 mmole) in formic acid (5 ml) was heated under reflux for 27 h. The reaction mixture was concentrated to a small volume and diluted with ice-cold water. The precipitate was filtered, washed with water and dried. Colourless crystals of the title compound were obtained by slow evaporation of a solution in aqueous ethanol.

S3.2. Refinement

The H atoms were included in calculated positions and treated as riding atoms: C—H = 0.93 - 0.98 Å with U_{iso}(H) = 1.5U_{eq}(C-methyl) and = 1.2U_{eq}(C) for other H atoms.

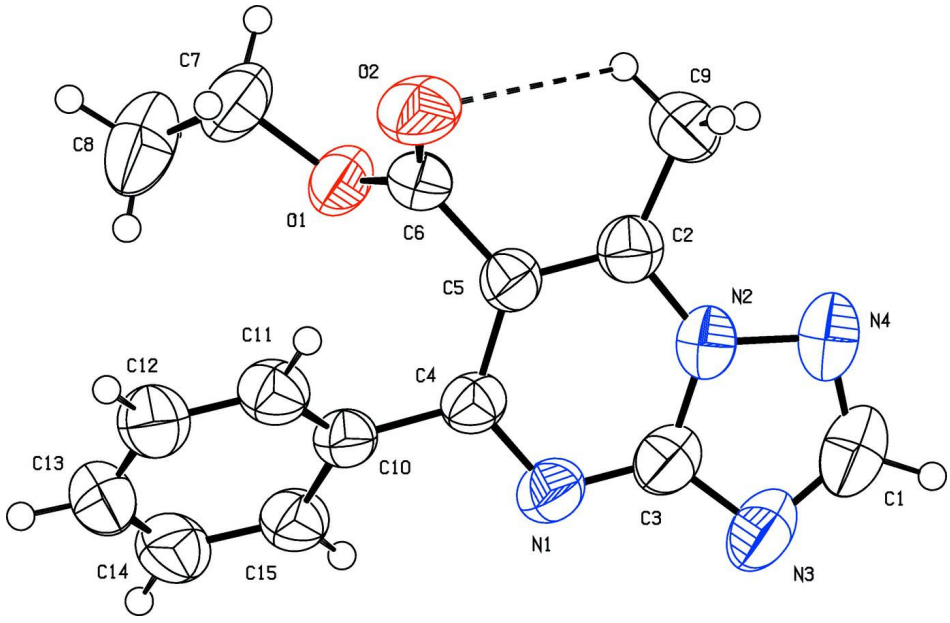

Figure 1

A view of the molecular structure of the title molecule, with atom labelling. Displacement ellipsoids are drawn at the 50% probability level. The intramolecular C—H···O hydrogen bond is shown as a dashed line (see Table 1 for details).

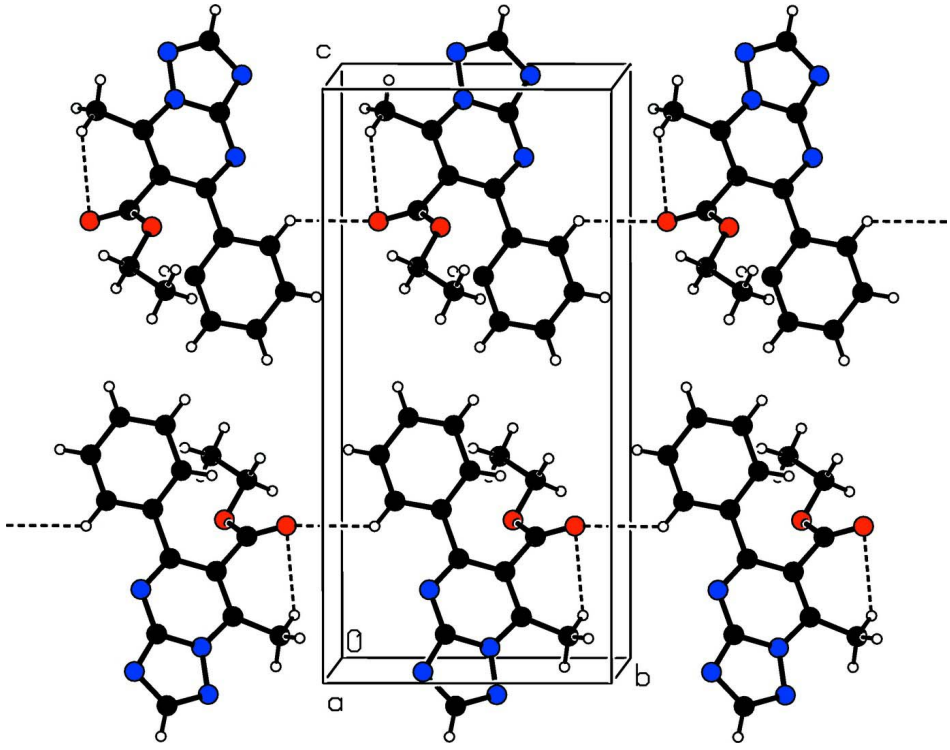

Figure 2

A view along the *a* axis of the crystal packing of the title compound. The C—H···O hydrogen bonds are shown as a dashed line (see Table 1 for details).

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Crystal data

$C_{15}H_{14}N_4O_2$
$M_r = 282.30$
Monoclinic, $P2_1/n$
$a = 10.322$ (2) Å
$b = 8.1678$ (19) Å
$c = 16.798$ (4) Å
$\beta = 92.111$ (4)°
$V = 1415.2$ (5) Å^3
$Z = 4$
$F(000) = 592$
$D_x = 1.325$ Mg m^{-3}
Mo $K\alpha$ radiation, $\lambda = 0.71075$ Å
Cell parameters from 10163 reflections
$\theta = 3.1$–$27.6°$
$\mu = 0.09$ mm^{-1}
$T = 293$ K
Prism, colourless
0.30 × 0.10 × 0.10 mm

Data collection

Rigaku SCXmini diffractometer
ω scans
Absorption correction: multi-scan (*REQAB*; Jacobson, 1998)
$T_{min} = 0.610$, $T_{max} = 0.991$
12066 measured reflections
2550 independent reflections
1742 reflections with $I > 2\sigma(I)$
$R_{int} = 0.092$
$\theta_{max} = 25.3°$, $\theta_{min} = 3.2°$
$h = -12 \rightarrow 12$
$k = -9 \rightarrow 9$
$l = -20 \rightarrow 20$

Refinement

Refinement on F^2
Least-squares matrix: full
$R[F^2 > 2\sigma(F^2)] = 0.076$
$wR(F^2) = 0.182$
$S = 1.07$
2550 reflections
193 parameters
0 restraints
Hydrogen site location: inferred from neighbouring sites
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.1047P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max} = 0.46$ e Å^{-3}
$\Delta\rho_{min} = -0.51$ e Å^{-3}
Extinction correction: *SHELXL2013* (Sheldrick, 2008), $Fc^* = kFc[1+0.001xFc^2\lambda^3/\sin(2\theta)]^{-1/4}$
Extinction coefficient: 0.118 (11)

Special details

Geometry. All e.s.d.'s (except the e.s.d. in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell e.s.d.'s are taken into account individually in the estimation of e.s.d.'s in distances, angles and torsion angles; correlations between e.s.d.'s in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell e.s.d.'s is used for estimating e.s.d.'s involving l.s. planes.

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å^2)

	x	*y*	*z*	U_{iso}*/U_{eq}
O1	0.39205 (15)	0.6185 (2)	0.24879 (9)	0.0632 (5)
O2	0.51731 (19)	0.8413 (2)	0.24434 (12)	0.0817 (6)
N1	0.68299 (18)	0.3481 (2)	0.14373 (12)	0.0619 (6)
N2	0.65225 (18)	0.5557 (3)	0.04523 (11)	0.0602 (6)
N3	0.7530 (2)	0.3301 (3)	0.00856 (15)	0.0811 (7)
N4	0.6793 (2)	0.5809 (3)	−0.03304 (12)	0.0763 (7)
C1	0.7390 (3)	0.4421 (4)	−0.04963 (18)	0.0844 (9)
H1A	0.7702	0.4229	−0.1000	0.101*
C2	0.5898 (2)	0.6607 (3)	0.09427 (14)	0.0571 (6)
C3	0.6971 (2)	0.4037 (3)	0.06930 (15)	0.0631 (7)
C4	0.6228 (2)	0.4455 (3)	0.19354 (13)	0.0514 (6)
C5	0.5725 (2)	0.6021 (3)	0.16969 (13)	0.0512 (6)
C6	0.4935 (2)	0.7029 (3)	0.22516 (14)	0.0557 (6)
C7	0.3199 (3)	0.6916 (4)	0.31288 (18)	0.0855 (9)
H7A	0.3792	0.7412	0.3520	0.103*
H7B	0.2621	0.7759	0.2917	0.103*
C8	0.2453 (3)	0.5624 (4)	0.3499 (2)	0.1047 (11)
H8A	0.1806	0.5220	0.3123	0.157*
H8B	0.2040	0.6054	0.3957	0.157*
H8C	0.3023	0.4746	0.3660	0.157*
C9	0.5465 (3)	0.8207 (3)	0.06000 (17)	0.0752 (8)
H9A	0.6189	0.8944	0.0591	0.113*
H9B	0.4806	0.8665	0.0921	0.113*
H9C	0.5122	0.8044	0.0067	0.113*
C10	0.6102 (2)	0.3845 (3)	0.27599 (13)	0.0518 (6)
C11	0.6315 (2)	0.4852 (3)	0.34188 (15)	0.0604 (7)
H11	0.6588	0.5925	0.3347	0.073*
C12	0.6127 (2)	0.4282 (3)	0.41738 (16)	0.0716 (8)

H12	0.6269	0.4969	0.4609	0.086*
C13	0.5726 (3)	0.2680 (4)	0.42890 (17)	0.0764 (8)
H13	0.5570	0.2304	0.4799	0.092*
C14	0.5560 (2)	0.1660 (3)	0.36494 (18)	0.0735 (8)
H14	0.5313	0.0579	0.3728	0.088*
C15	0.5757 (2)	0.2217 (3)	0.28853 (15)	0.0594 (7)
H15	0.5659	0.1505	0.2455	0.071*

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
O1	0.0658 (10)	0.0599 (10)	0.0652 (11)	−0.0005 (8)	0.0222 (8)	−0.0063 (8)
O2	0.0989 (14)	0.0453 (11)	0.1024 (15)	0.0022 (9)	0.0206 (11)	−0.0087 (9)
N1	0.0677 (12)	0.0523 (12)	0.0665 (14)	0.0044 (10)	0.0151 (10)	−0.0045 (10)
N2	0.0599 (12)	0.0686 (14)	0.0527 (12)	−0.0042 (10)	0.0113 (9)	0.0021 (10)
N3	0.0879 (16)	0.0836 (17)	0.0737 (16)	−0.0003 (13)	0.0294 (12)	−0.0176 (13)
N4	0.0772 (14)	0.0967 (18)	0.0560 (14)	−0.0106 (13)	0.0176 (11)	0.0007 (13)
C1	0.088 (2)	0.100 (2)	0.0668 (19)	−0.0110 (18)	0.0246 (15)	−0.0165 (18)
C2	0.0522 (13)	0.0566 (15)	0.0629 (16)	−0.0033 (11)	0.0078 (11)	0.0020 (12)
C3	0.0631 (15)	0.0613 (16)	0.0658 (17)	−0.0007 (12)	0.0139 (12)	−0.0080 (13)
C4	0.0514 (12)	0.0438 (13)	0.0594 (15)	−0.0020 (10)	0.0069 (10)	−0.0040 (11)
C5	0.0534 (13)	0.0459 (13)	0.0549 (14)	−0.0033 (10)	0.0091 (10)	0.0008 (10)
C6	0.0640 (14)	0.0447 (14)	0.0588 (14)	0.0064 (11)	0.0079 (11)	0.0044 (11)
C7	0.092 (2)	0.082 (2)	0.085 (2)	0.0076 (16)	0.0389 (16)	−0.0107 (16)
C8	0.110 (2)	0.115 (3)	0.092 (2)	−0.026 (2)	0.0457 (19)	−0.0211 (19)
C9	0.0748 (16)	0.0750 (19)	0.0764 (19)	0.0108 (14)	0.0102 (13)	0.0226 (14)
C10	0.0540 (13)	0.0447 (13)	0.0571 (14)	0.0039 (10)	0.0076 (10)	0.0006 (11)
C11	0.0666 (15)	0.0505 (14)	0.0639 (16)	−0.0002 (11)	−0.0017 (12)	−0.0025 (12)
C12	0.0791 (17)	0.0751 (18)	0.0602 (17)	0.0074 (14)	−0.0033 (13)	−0.0020 (14)
C13	0.0807 (18)	0.084 (2)	0.0649 (17)	0.0115 (16)	0.0091 (13)	0.0192 (16)
C14	0.0725 (17)	0.0602 (17)	0.089 (2)	0.0006 (13)	0.0147 (15)	0.0154 (15)
C15	0.0653 (14)	0.0440 (13)	0.0696 (16)	0.0002 (11)	0.0109 (12)	0.0017 (12)

Geometric parameters (Å, º)

O1—C6	1.327 (3)	C7—H7B	0.9700
O1—C7	1.459 (3)	C8—H8A	0.9600
O2—C6	1.198 (3)	C8—H8B	0.9600
N1—C4	1.325 (3)	C8—H8C	0.9600
N1—C3	1.343 (3)	C9—H9A	0.9600
N2—C2	1.367 (3)	C9—H9B	0.9600
N2—N4	1.370 (3)	C9—H9C	0.9600
N2—C3	1.380 (3)	C10—C11	1.390 (3)
N3—C3	1.334 (3)	C10—C15	1.395 (3)
N3—C1	1.343 (4)	C11—C12	1.372 (3)
N4—C1	1.325 (4)	C11—H11	0.9300
C1—H1A	0.9300	C12—C13	1.388 (4)
C2—C5	1.372 (3)	C12—H12	0.9300

C2—C9	1.490 (3)	C13—C14	1.365 (4)
C4—C5	1.432 (3)	C13—H13	0.9300
C4—C10	1.482 (3)	C14—C15	1.384 (3)
C5—C6	1.506 (3)	C14—H14	0.9300
C7—C8	1.459 (4)	C15—H15	0.9300
C7—H7A	0.9700		

C6—O1—C7	116.0 (2)	C7—C8—H8A	109.5
C4—N1—C3	117.0 (2)	C7—C8—H8B	109.5
C2—N2—N4	127.0 (2)	H8A—C8—H8B	109.5
C2—N2—C3	123.3 (2)	C7—C8—H8C	109.5
N4—N2—C3	109.8 (2)	H8A—C8—H8C	109.5
C3—N3—C1	102.2 (3)	H8B—C8—H8C	109.5
C1—N4—N2	100.7 (2)	C2—C9—H9A	109.5
N4—C1—N3	117.9 (3)	C2—C9—H9B	109.5
N4—C1—H1A	121.0	H9A—C9—H9B	109.5
N3—C1—H1A	121.0	C2—C9—H9C	109.5
N2—C2—C5	114.7 (2)	H9A—C9—H9C	109.5
N2—C2—C9	117.3 (2)	H9B—C9—H9C	109.5
C5—C2—C9	128.0 (2)	C11—C10—C15	118.5 (2)
N3—C3—N1	128.6 (3)	C11—C10—C4	121.9 (2)
N3—C3—N2	109.4 (2)	C15—C10—C4	119.6 (2)
N1—C3—N2	122.0 (2)	C12—C11—C10	120.8 (2)
N1—C4—C5	122.2 (2)	C12—C11—H11	119.6
N1—C4—C10	116.6 (2)	C10—C11—H11	119.6
C5—C4—C10	121.20 (18)	C11—C12—C13	120.1 (3)
C2—C5—C4	120.8 (2)	C11—C12—H12	119.9
C2—C5—C6	118.2 (2)	C13—C12—H12	119.9
C4—C5—C6	120.97 (19)	C14—C13—C12	119.7 (3)
O2—C6—O1	124.5 (2)	C14—C13—H13	120.2
O2—C6—C5	124.9 (2)	C12—C13—H13	120.2
O1—C6—C5	110.6 (2)	C13—C14—C15	120.7 (3)
C8—C7—O1	108.1 (2)	C13—C14—H14	119.6
C8—C7—H7A	110.1	C15—C14—H14	119.6
O1—C7—H7A	110.1	C14—C15—C10	120.0 (2)
C8—C7—H7B	110.1	C14—C15—H15	120.0
O1—C7—H7B	110.1	C10—C15—H15	120.0
H7A—C7—H7B	108.4		

C2—N2—N4—C1	−179.8 (2)	C10—C4—C5—C2	177.0 (2)
C3—N2—N4—C1	−0.3 (2)	N1—C4—C5—C6	174.1 (2)
N2—N4—C1—N3	0.3 (3)	C10—C4—C5—C6	−6.1 (3)
C3—N3—C1—N4	−0.2 (3)	C7—O1—C6—O2	−11.1 (3)
N4—N2—C2—C5	178.28 (19)	C7—O1—C6—C5	170.1 (2)
C3—N2—C2—C5	−1.2 (3)	C2—C5—C6—O2	−58.0 (3)
N4—N2—C2—C9	−0.4 (3)	C4—C5—C6—O2	125.1 (3)
C3—N2—C2—C9	−179.9 (2)	C2—C5—C6—O1	120.8 (2)
C1—N3—C3—N1	−179.8 (3)	C4—C5—C6—O1	−56.1 (3)

C1—N3—C3—N2	0.0 (3)	C6—O1—C7—C8	−159.8 (2)
C4—N1—C3—N3	−179.8 (2)	N1—C4—C10—C11	137.2 (2)
C4—N1—C3—N2	0.5 (3)	C5—C4—C10—C11	−42.6 (3)
C2—N2—C3—N3	179.8 (2)	N1—C4—C10—C15	−42.9 (3)
N4—N2—C3—N3	0.2 (3)	C5—C4—C10—C15	137.3 (2)
C2—N2—C3—N1	−0.4 (4)	C15—C10—C11—C12	−3.2 (3)
N4—N2—C3—N1	−180.0 (2)	C4—C10—C11—C12	176.6 (2)
C3—N1—C4—C5	1.1 (3)	C10—C11—C12—C13	0.3 (4)
C3—N1—C4—C10	−178.75 (19)	C11—C12—C13—C14	2.2 (4)
N2—C2—C5—C4	2.6 (3)	C12—C13—C14—C15	−1.7 (4)
C9—C2—C5—C4	−178.8 (2)	C13—C14—C15—C10	−1.3 (4)
N2—C2—C5—C6	−174.28 (19)	C11—C10—C15—C14	3.7 (3)
C9—C2—C5—C6	4.3 (4)	C4—C10—C15—C14	−176.1 (2)
N1—C4—C5—C2	−2.8 (3)		

Hydrogen-bond geometry (Å, º)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
C9—H9*B*···O2	0.96	2.58	3.127 (4)	116
C15—H15···O2^{i}	0.93	2.57	3.246 (3)	129

Symmetry code: (i) *x*, *y*−1, *z*.